*Osteoarthritis and Cartilage* (1999) **7,** 427–429

Article No. joca.1998.0233, available online at http://www.idealibrary.com on IDEAL®
1063–4584/99/040427+03 $12.00/0

**Osteoarthritis and Cartilage**
Journal of the OsteoArthritis Research Society International

# Radiographic assessment. Introduction: existing methodology

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## Summary

Plain radiograph is the most accepted imaging technique to assess structural changes of osteoarthritis and it is proposed as 'surrogate' of outcome of the disease process. The existing radiographic methodology is well standardized with respect to its technique for investigation of hip, knee and hand joints, including advice on the most appropriate views, patient positioning, X-ray beam alignment, quality control. Quantitation of joint space narrowing is currently proposed as the primary variable in studies of disease progression for hip and knee, while semi-quantitation of this same parameter or of bone changes by published atlases have to be intended as secondary variables, or outcomes in hand studies. Unfortunately, the review of studies that evaluated the longitudinal rate of joint space narrowing indicates that the yearly change may be very small (<0.1 mm/year) and of doubtful clinical significance. This underlines the need for further refinement in the definition of the radiographic outcome in prospective clinical trials.

*Key words*: Osteoarthritis, Hip, Knee, X-ray.

## Introduction

Disease outcome measurement in osteoarthritis (OA) includes different possibilities: (a) ideally, measurement of the real disease process, that could be obtained only by pathology assessment; (b) measures of joint pain and disability, or (c) imaging measurement of joint structural changes. In the impossibility of performing a pathology assessment, the remaining two alternatives should be used. Although clinical measures are probably the best indicator of the disease and of the activity of a drug, as well as those most easily appreciated by physicians and patients, they may be influenced in the long run by different other factors. Furthermore, the development of severe disability, i.e., of the disease final outcome, may not be easy to determine (e.g., the inadequacy of parameters such as the frequency of joint arthroplasty). Plain radiograph is at present the most economical, easily available and accepted imaging technique to assess structural changes of OA. It is currently proposed as 'surrogate' of outcome of the disease process, provided that the existing methodology is sufficiently standardized, but also that it can reasonably be correlated with symptom change, as currently required by Regulatory Agencies such as the FDA[1] or the EMEA[2] and/or the outcome is clinically relevant.

## Standardization of the existing methodology

The levels of standardization of the existing radiographic methodology include the technique, the evaluation variables and the outcome. Much of the effort during the recent years has been placed on the standardization of the technique, in order to limit the sources of variability in measurement and interpretation, including: patient positioning, the radiographic procedure (e.g., centering of the X-ray focal spot, the focus–film distance, etc.), the measurement process. Different documents have been produced in this regard, either by scientific bodies such as the OsteoArthritis Research Society International (OARSI),[3] or the American Academy of Orthopaedic Surgeons in conjunction with the WHO,[4] or by individual Authors (e.g.,[5,6]) and they are concerned with the three major joints that are today considered the target of investigation, namely the hip, knee and hand. Several basic aspects are now standard in the radiographic procedure, such as the use of a fast screen, cassette film and a focus to film distance of 100 cm. With regard to patient positioning, it should be noted that the use of fluoroscopy is recommended for a correct X-ray beam alignment. Furthermore, hand supports should be provided in some positions for patient's stability and foot (or hand) maps may be useful for repositioning and reproducibility (although even a multipoint control may be needed in some instances, e.g., to avoid body torque about the knee in the weight-bearing assessment of the hip). For studies involving the hip or the knee, the current preference goes to weight-bearing (standing) anteroposterior views of one or both joints. However, still there may be discussions on the possibility of accepting hip views with the patient lying on the table and the feet internally rotated, since the latter appears to apply a load to the articular surface, possibly obviating the need for weight-bearing films.[4] Similarly, work is still needed to define if the tibiofemoral compartment of the knee should be better investigated in the fully extended view or in the partially flexed view. Conversely, sufficient agreement exists on the investigation of the patellofemoral compartment of the knee by the skyline (also known as axial, or sunrise, or sunset) view of each knee and for the dorsopalmar view of the wrist and hand. Details about patient positioning and X-ray beam alignment are given elsewhere.[3,4] Correction for radiographic magnification has been shown to improve accuracy and precision of measurements, especially for the hip and knee, since the distance between the joint and the film may vary among individuals, or for each individual if significant weight

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change occurs between visits.[5] Finally, the need for central reading, quality and reproducibility testing, as well as for appropriate training of radiologists and technicians, is acknowledged.

## The evaluation variables

Ideally, global radiographic scales would be a perfect evaluation variable, since they would consider both cartilage loss (joint space narrowing) and the bone response (osteophytes, sclerosis, cysts, etc.) and may be used for both disease diagnosis (and its staging) and disease progression (and the grading of this progression). The Kellgren and Lawrence scale[7] has been the first and most widely used of these attempts. However, the limits inherent to the scale and to its implementation[8] have favoured the return to the evaluation of individual radiographic features and their separate quantitation, or at least semi-quantitation. Currently, a prominent feature such as joint space narrowing (JSN) can be precisely quantitated in tenths of mm by ruler, calliper and/or a graded magnifying lens.[9] Precision may be improved by digitalization and computerized techniques of image analysis. Although similar quantitative methodologies may be applied for bone response features, semiquantitative grading on a 0–3 scale has been proposed as a more standardized alternative for most of them (osteophytes, subchondral sclerosis and cysts, etc.) and for JSN itself, resulting in the creation of new atlases that can be easily used for standardization.[10] Whatever the selected variable, this should be separately assessed for each joint compartment.[10]

Scientific and regulatory agreement apparently exists on the OARSI[3] and GREES[11] proposal of using the measurement of JSN at the joint narrowest point as primary variable in studies of disease progression for hip and knee, while osteophytes and other bone changes should be regarded as secondary variables. Conversely, studies of prevention may better focus on osteophytes, since they are most strongly associated with pain, at least at the knee, and they are a basic component of the ACR classification criteria.[12] Radiographic outcomes in studies of the hand should probably be based on predetermined features described in published atlases, in the absence of sufficient standardization of more precise variables.

## Significance of the radiographic outcome

Published longitudinal studies evaluating the rate of JSN at the knee joint have been recently reviewed.[13] Although most of these studies are questionable for different reasons, i.e., the short duration of follow-up for some of them, or the small number of patients for others, or the inclusion of patients with different degrees of risk factors for progression, the rate of JSN varies greatly. Several discussions could by made for the differences in technique and standardization, but there is a clear indication that the overall change in JSN may be much less than previously expected and very small (<0.1 mm/year). Indeed, this has been recently confirmed by two studies of appropriate size and duration, one targeted to the investigation of the natural history of OA in a very selected patient group[14] and the other reporting the results of the placebo arm of a randomised double-blind trial of a putative Structure Modifying Drug.[15] In both studies the average rate of JSN was about 0.08 mm/year. The clinical significance of such a small change is doubtful and indeed the correlation between radiographic progression and symptom progression was poor.[14] The clear definition of the radiographic outcome to be pursued in trials of Structure Modifying Drugs in OA and its validity, is therefore the weak point in the existing methodology. The view of Regulatory Agencies may be that until when its standardized clinical significance is proven in randomized, placebo-controlled, double-blind studies, it may remain ancillary to clinical outcomes.[1,2]

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